



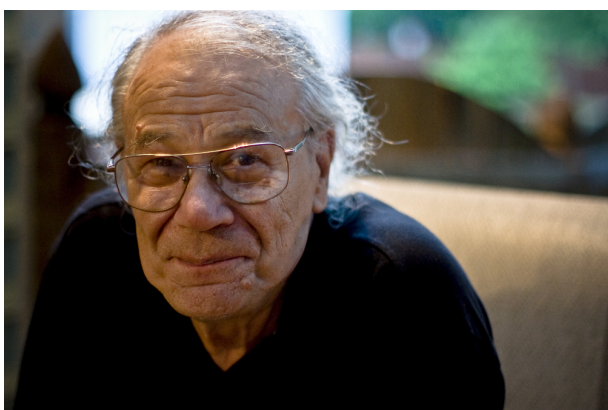
OBITUARIES

John “Mickey” Nardo

Pioneer in trial reanalysis

Bob Roehr

Washington, DC



[Image: Credit: Abby Nardo]

The name Mickey Nardo is not widely known, but it should be. Nardo played a yeoman’s role in the first-of-its-kind 2015 reanalysis of Study 329,¹ which used industry data to show that the selective serotonin reuptake inhibitor paroxetine (Paxil, Seroxat) had no beneficial effect and caused substantial harm when used to treat major depression in adolescents.

Nardo always thought he wanted to do research, but his path ended up being long and circuitous, with many rewarding chapters along the way.

Early career

He focused on mathematics at the University of Tennessee, Knoxville, and continued at the university school of medicine in Memphis, obtaining his MD in 1967. Residencies in internal medicine, and immunology and rheumatology followed, with the aim of going into research. An offer from Stanford University to work on tissue typing for organ transplant was pending, when a letter from the Pentagon arrived.

As the war in Vietnam raged, Nardo was offered the choice of serving two years at a hospital in Abilene, Texas, or three years in England. “We didn’t have to think one nanosecond about that,” recalls his wife, Sharon. The young family, which by now included baby Abby, moved to RAF Lakenheath Hospital in

Suffolk in 1971, where the paterfamilias served as chief of internal medicine.

The big revelation for Nardo was that he really liked working with patients, particularly talking with them and dealing with psychosomatic issues. The idea of a career in research faded, and on his return to the US he began a residency in psychiatry at Emory University in Atlanta, and later commuted for seven years to train at the Columbia Psychoanalytic Institute in New York City.

Psychiatric pharmacology

Psychiatric pharmacology was on the rise, embodied at Emory by a new department chair, “Mickey just couldn’t make that switch,” says Sharon, “he and the new chairman did not get along at all.” He left a tenured position in 1986 and went into private practice, although he continued to teach at the Emory Psychoanalytic Institute until his death.²

Mickey’s parents both died before reaching 65, and he decided to retire from regular clinical practice in 2003, “to enjoy the rest of his life.” The deal he struck with Sharon was to sell their house in Atlanta and use a bucolic vacation place in Jasper, Georgia, as their base while they travelled to China, India, Kenya, the Galapagos, and other exotic locales.

From “serial hobbyist” to the RIAT initiative

Nardo had been “a serial hobbyist” who would pick up one thing—early computers built from kits, photography, blacksmithing—master it, and move on. So it was no surprise that in retirement he took up blogging (<http://1boringgoldman.com>).

At first his blog was primarily political, but volunteer work at a local charity clinic brought him into contact with mainstream psychiatric patients. These were very different from the patients he had seen in his analytic clinical practice. Nardo was shocked and horrified by the high dosages and inappropriate use of drugs prescribed for psychiatric conditions, often with questionable evidence regarding their efficacy. His posts increasingly covered those issues and soon caught the eye of other psychiatrists; he

was asked to join the RIAT initiative,^{3,4} the group re-examining the Study 329 data.

The US Food and Drug Administration had approved an indication of paroxetine to treat depression in adolescents in 2001. It was based in part on Study 329,⁵ which quickly generated controversy over issues of efficacy, safety, and questionable practices in writing the paper and using it for marketing.⁶

GlaxoSmithKline would later pay billions of dollars in fines to settle lawsuits over the drug. As part of a legal settlement it agreed to make raw data from the study available to researchers.

But access to the 77 000 pages of patient reports was strictly online, and the re-examination team was not allowed to download or even print out the material. They likened their view to that through a periscope.

Nardo took on much of the task of reviewing individual patients' reports and coding them according to the standards of the *Medical Dictionary for Regulatory Activities*, then entering the data into a useable format. The process was long and tedious. He also drew on his mathematical background for the analysis.

Peer review can be an extensive process, particularly if an intervention or analysis is the first of its kind, as was this reanalysis. While some coauthors chaffed at the process, "Mickey didn't get caught up in it. He had a passion, but he was also calm about it," said Peter Doshi, who helped to mediate between the authors and *The BMJ*'s editors. Doshi would later become an assistant professor at the University of Maryland School of Pharmacy and an associate editor at *The BMJ*.

The reanalysis found that, contrary to the initial finding, using paroxetine for this indication did not confer any benefit. More importantly, harm in terms of suicidal ideation was increased when one looked at the continuation phase and in the context of parallel trials. Many have called for the original Study 329 paper to be retracted, so far unsuccessfully.

The impact of the reanalysis on clinical practice was minimal because preceding controversies had already steered doctors and patients away from paroxetine. "The impact was more symbolic," says Doshi. "It was a repudiation that the company is able to always control the message. It switched the scenario from safe and effective to ineffective and unsafe." He hopes the

paper will serve as an example to others, to reanalyse trial data that are increasingly being made public, but he acknowledges that such work takes much time and effort; it is not likely to occur until funding becomes available to conduct reanalyses.

The key message from the reanalysis lay in its concluding paragraph: "As with most scientific papers, Keller and colleagues convey an impression that 'the data have spoken.' This authoritative stance is possible only in the absence of access to the data. When the data become accessible to others, it becomes clear that scientific authorship is provisional rather than authoritative."

At the time of his death, Nardo was working on a petition to stop false reporting of drug benefits and harms. www.change.org/p/congress-congress-stop-false-reporting-of-drug-benefits-harms-by-making-fda-nih-work-together

Nardo was born in Chattanooga, Tennessee, and died in Atlanta, Georgia. He leaves his wife, Sharon; and a daughter, Abby, a psychologist practising in Raleigh, North Carolina. A celebration of his life will be held in Atlanta on 18 March, check the blog for the exact time and location.

Biography

John Michael "Mickey" Nardo (b 1941; q Memphis 1967), died from pneumonia complicated by a lifetime of smoking on 19 February 2017

- 1 Le Noury J, Nardo JM, Healy D, et al. Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence. *BMJ* 2015;351:h4320. doi:10.1136/bmj.h4320pmid:26376805.
- 2 Hopkins Tanne J. US university psychiatrist loses chairmanship over drug company payments. *BMJ* 2009;338:a3188. doi:10.1136/bmj.a3188pmid:19126618.
- 3 Loder E, Godlee F, Barbour V, Winker M. PLOS Medicine editors. Restoring the integrity of the clinical trial evidence base. *BMJ* 2013;346:f3601. doi:10.1136/bmj.f3601pmid:23766484.
- 4 Doshi P, Dickersin K, Healy D, Vedula SS, Jefferson T. Restoring invisible and abandoned trials: a call for people to publish the findings. *BMJ* 2013;346:f2865. doi:10.1136/bmj.f2865pmid:23766480.
- 5 Keller MB, Ryan ND, Strober M, et al. Efficacy of paroxetine in the treatment of adolescent major depression: a randomized, controlled trial. *J Am Acad Child Adolesc Psychiatry* 2001;40:762-72. doi:10.1097/00004583-200107000-00010pmid:11437014.
- 6 Study 329. 2017. https://en.wikipedia.org/wiki/Study_329.

Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to <http://group.bmj.com/group/rights-licensing/permissions>